CLAIMS

1. A combination which comprises (a) an aromatase inhibitor and (b) a bisphosphonate in which the active ingredients (a) and (b) are present in each case in free form or in the form of a pharmaceutically acceptable salt, for simultaneous, concurrent, separate or sequential use in the prevention of bone loss which is caused by the treatment with an aromatase inhibitor of a disease or condition which responds to aromatase inhibition.

2. A method of treating a patient suffering from a disease or condition which responds to aromatase inhibition comprising administering to the patient an effective amount of a bisphosphonate and an effective amount of an aromatase inhibitor, especially with the proviso that the patient is not additionally treated with a chemotherapeutic agent.

3. The method of claim 2 for the treatment of a proliferative disease.

4. Use of an aromatase inhibitor for the preparation of a medicament, for use in combination with a bisphosphonate for treatment of a disease or condition which responds to aromatase inhibition, especially with the proviso that the disease or condition is not additionally treated with a chemotherapeutic agent.

5. Use of an aromatase inhibitor for the preparation of a medicament, for use in combination with a bisphosphonate for prevention of bone loss which is caused by the treatment with an aromatase inhibitor of a disease or condition which responds to aromatase inhibition.

6. Use of a bisphosphonate for the preparation of a medicament, for use in combination with an aromatase inhibitor for treatment of a disease or condition which responds to

aromatase inhibition, especially with the proviso that the disease or condition is not additionally treated with a chemotherapeutic agent.

7. Use of a bisphosphonate for the preparation of a medicament, for use in combination with an aromatase inhibitor for prevention of bone loss which is caused by the treatment with an aromatase inhibitor of a disease or condition which responds to aromatase inhibition.

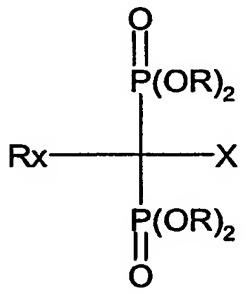
8. The use according to any one of claims 4-7 for treatment of a proliferative disease.

9. A package comprising a bisphosphonate together with instructions for use in combination with an aromatase inhibitor for treatment of a disease or condition which responds to aromatase inhibition, especially with the proviso that the disease or condition is not additionally treated with a chemotherapeutic agent, or
a package comprising an aromatase inhibitor together with instructions for use in combination with a bisphosphonate for treatment of a disease or condition which responds to aromatase inhibition, especially with the proviso that the disease or condition is not additionally treated with a chemotherapeutic agent.

10. A package comprising a bisphosphonate together with instructions for use in combination with an aromatase inhibitor for prevention of bone loss which is caused by the treatment with an aromatase inhibitor of a disease or condition which responds to aromatase inhibition, or
a package comprising an aromatase inhibitor together with instructions for use in combination with a bisphosphonate for prevention of bone loss which is caused by the treatment with an aromatase inhibitor of a disease or condition which responds to aromatase inhibition.

11. The combination according to claim 1, method according to claim 2 or 3, use according to any one of claims 4-8, or package according to claim 9 or 10, in which the bisphosphonate is an N-bisphosphonate.

12. The combination, method, use or package according to claim 11 in which the bisphosphonate is a compound of formula I



I

wherein

X is hydrogen, hydroxyl, amino, alkanoyl, or an amino group substituted by C_1-C_4 alkyl, or alkanoyl;

R is hydrogen or C_1-C_4 alkyl and

Rx is a side chain which contains an optionally substituted amino group, or a nitrogen containing heterocycle (including aromatic nitrogen-containing heterocycles),

or a pharmaceutically acceptable salt thereof or any hydrate thereof.

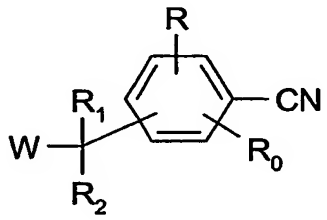
13. The combination, method, use or package according to claim 12, in which the bisphosphonate is 2-(imidazol-1yl)-1-hydroxyethane-1,1-diphosphonic acid (zoledronic acid) or a pharmaceutically acceptable salt thereof.

14. The combination according to claim 1, method according to claim 2 or 3, use according to any one of claims 4-8, or package according to claim 9 or 10, in which the aromatase inhibitor is selected from exemestane, formestane, aminoglutethimide, vorozole,

fadrozole, anastrozole, letrozole, roglethimide, pyridoglutethimide, trilostane, testolactone, atamestane, 1-methyl-1,4-androstadiene-3,17-dione, ketokonazole and pharmaceutically acceptable salts of these compounds.

15. The combination, method, use or package according to claim 14, in which the aromatase inhibitor is selected from exemestane, formestane, aminoglutethimide, fadrozole, anastrozole, letrozole and pharmaceutically acceptable salts of these compounds.

16. The combination according to claim 1, method according to claim 2 or 3, use according to any one of claims 4-8, or package according to claim 9 or 10, in which the aromatase inhibitor is a compound of formula I



(I)

wherein R and R_0, independently of one another, are each hydrogen or lower alkyl, or R and R_0 at adjacent carbon atoms, together with the benzene ring to which they are bonded, form a naphthalene or tetrahydronaphthalene ring; wherein R_1 is hydrogen, lower alkyl, aryl, aryl-lower alkyl or lower alkenyl; R_2 is hydrogen, lower alkyl, aryl, aryl-lower alkyl, (lower alkyl, aryl or aryl-lower alkyl)-thio or lower alkenyl, or wherein R_1 and R_2 together are lower alkylidene or C_4-C_6alkylene; wherein W is 1-imidazolyl, 1-(1,2,4 or 1,3,4)-triazolyl, 3-pyridyl or one of the mentioned heterocyclic radicals substituted by lower alkyl; and aryl within the context of the above definitions has the following meanings: phenyl that is unsubstituted or substituted by one or two substituents from the group lower alkyl, lower alkoxy, hydroxy, lower alkanoyloxy, nitro, amino, halogen, trifluoromethyl, cyano, carboxy, lower alkoxycarbonyl,

carbamoyl, N-lower alkylcarbamoyl, N,N-di-lower alkylcarbamoyl, lower alkanoyl, benzoyl, lower alkylsulfonyl, sulfamoyl, N-lower alkylsulfamoyl and N,N-di-lower alkylsulfamoyl; also thienyl, indolyl, pyridyl or furyl, or one of the four last-mentioned heterocyclic radicals monosubstituted by lower alkyl, lower alkoxy, cyano or by halogen; or a pharmaceutically acceptable salt thereof.

17. The combination, method, use or package according to claim 16 in which the aromatase inhibitor is 4-[α-(4-cyanophenyl)-1-(1,2,4-triazolyl)methyl]-benzonitrile (letrozole) or a pharmaceutically acceptable salt thereof.

18. A method of preventing bone loss in a patient suffering from an estrogen dependent disorder and receiving an aromatase inhibitor comprising administering to said patient an effective amount of a bisphosphonate.

19. A method of preventing cancer treatment-related bone loss in a postmenopausal woman with ER+ and/or PR+ breast cancer receiving an aromatase inhibitor as adjuvant therapy comprising administering to said postmenopausal woman an effective amount of a bisphosphonate.

20. The method according to claim 18 or 19 wherein the bisphosphonate is an N-bisphosphonate.

21. The method according to claim 20 wherein the N-bisphosphonate is zoledronic acid or a pharmaceutically acceptable salt thereof.

22. The method according to any one of claims 18-21 wherein the aromatase inhibitor is letrozole or a pharmaceutically acceptable salt thereof.

23. The method according to any one of claims 18-22 wherein the bisphosphonate is administered once every six months.